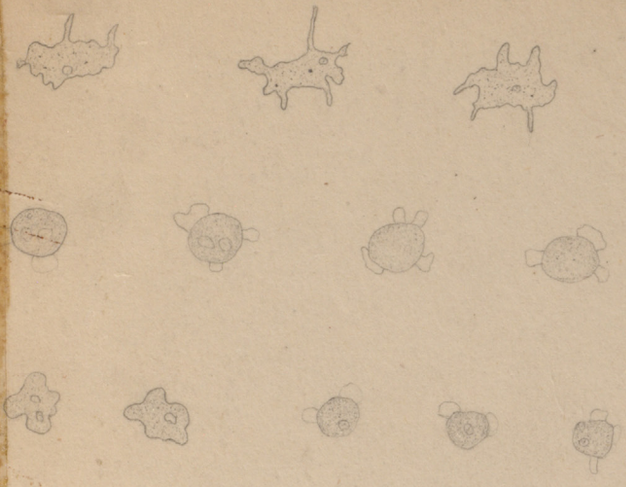
~~Osler~~
WG.6

7640. ‘The action of certain reagents—Atropia, Physostigma, Curare—on the white blood corpuscles’; 3 MS. drafts; 1873.

“My first scientific paper . . . read (with many vasomotor accompaniments)” before the Medical Microscopical Society, London (Osler, no. 6349). Published, in part, in Quarterly Jrnl. Micr. Sci., Lond., 1873, n.s. vol. 13, pp. 307–9; &c.

7640



These figures are all that remain of a research which cost several months work - an attempt to determine on the leucocytes the antagonistic action of atropia and physostigmin, an article on which - the general antagonism - has recently appeared by Thomas Fraser. It did not come a very much, but the first paper I read was before the Medical Microscopical Society in May 1874 (in a state I remember of Falstaffian "dis-solution & thaw") There is a note upon it in Proceedings & Trans. The Quarterly Jr. Micros. Science

various hyaline processes which I term out by the leucocytes ... these figures represent probably physical effects. It was while working at this subject that my attention was called to the Schultzes granules, masses & the blood platelets

W.D.

I - 8

Found 1945 in Cushing's material, #8303.

Reproduced in the "Life" 1st ed., 6/p. p. 104.

W.W.

7640.
Atropia
blood c
" My
vasomot
Microsco
Publishe
Lond., 1

7640

(1) Normal process. Newts blood
(2) Forms assume a tripolate corpuscle of Newt with 1% atropine at 10', 20', 30', 50' Many intermediate forms of course recorded
(3) Curious form of process, Frogs blood 1% atropia
(4) Human blood. Changes in five minutes. 1% atropia
(5) Human blood. Physostigmia 1%. Changes in five minutes
(6) Normal hyaline process from Newts blood
(7) Granular corpuscle of Human blood showing clear protoplasm devoid of any granules.

Found 1945 in
Cushing's material, #F303
W.W.T.

(foll. 1, & 30 – 2 drafts + notes &c?)

Three drafts of

"The Action of Certain Reagents – Atropia, Physostigma, Curare – on the White Blood Corpuscles"

published in abstract, Quart. J. Micr. Sc., Lond.

1873. n.s. xiii. pp 307-09 [& elsewhere.]

"The action of certain reagents – Atropia, Physostigma. Curare – on the white blood corpuscles"

Jour. Microsc. Q. J. M. S. 1873
p 307.

The preparations used were the Sulphate of Atropia, a somewhat impure Sulphate of Physostigma, which was kindly furnished by Prof. Fraser of Edinburgh, and ordinary Curare as obtained from Messrs Hopkins & Williams

Fresh solutions of Atropine were always employed, of the Physostigma as ~~1/2~~ 1 cc of 1% was made at a time, & a rather larger quantity of Curare, all the solutions were made with the saline

The blood used was of Man, Newt & Frog

The method of conducting the experiments was as follows: for the Newt & Frog the proportion between the blood & solutions was not accurately measured, but about one part the ~~quantity~~ of blood was added to the reagent on a slide & both carefully mixed. the corpuscles of which, such as are recognized by alterations in form, constitution &c and ~~we may premise~~, occur a

Hyaline processes in protoplasmic masses are by no means uncommon, indeed protoplasm may I take it be considered in its most typical form to be hyaline & as such we know it in the pseudopod. of the Rhizopods & in the ectosarc of the Amoeba &c

If we want seek a counterpart to this ~~clear~~ hyaline protoplasm we find one in the blood lymph it in the granular white blood corpuscles. I would here remark in passing that I find there – in my own blood at least – a constant element & since my attention was drawn to them I have rarely examined a specimen without finding one or two (Cont on back of P. 2

Newts no reagent 144 . 5 Hyaline } 271 & 12 Hy
" with saline 127 7 Hyaline.

Frogs no reagent 182 3 Hyaline } 319 & 10 Hy
with saline 137 7 Hyaline

Human no reag 97 } 187 & none hyaline
Human saline 90

Atropine in strength 1 t

after applying the cover slip being removed by filter paper. For the human blood, the proportion of ~~four~~ fifths of reagent to one fifth blood was kept used, both being measured in capillary pipette, ~~and~~ after mixing, the preparation was surrounded with oil and maintained during observation at a temperature between 37° & 39°C in a Stricker's stage or Dr Schafer modification

The experiments with atropia and Physostigmin were undertaken with a view of demonstrating if possible ~~for~~ on the white blood corpuscles, the ~~same~~ antagonism between these substances which ~~as~~ has been so ably shown to exist by Dr Fraser. In this, as you will hear, I have failed and am concerned now alone, with the effects they produce

The reagents which are credited with definite actions on the blood corpuscles produce their effect through physical changes, which are recognized by alterations in form, constitution &c and ~~we may presume~~, occur a

They consist of a clear protoplasm in which large dark granules are imbedded, but it rarely happens, however, that these granules entirely fill it even, the corpuscle, a clear space is usually left which, especially when the corpuscle at rest is in the centre, looks like a nucleus or a vacuole, but in some cases this clear spot may represent such, but if you watch one in active movement to spread out in the cover glass then you may see that - as in pus - the hyaline protoplasm usually forms the pseudopodia or undulating thin membranous and into it the dark granules stream

Atropine in strengths between 1:3000 & 2000
1.000 permits the natural movement
of the corpuscles to [illegible] unchecked, though
the duration is diminished, still with
1:1000 some may be noticed in motion two
hours or half after the application of the re-
agent. Solutions between 1:1000 & 1:3000 & 4000
lessen the activity and duration of the move-
ments, & some time attenuates them entirely solut-
ions ranging from 1:500 to 2d 3 & 4000 definitely
change the character of the movements & the
shape of the process
The forms assumed by the colourless elements
depend on the presence of numerous processes
which many changes in structure appearance
are identical with the body of the corpuscles
from which they spring
The attenuation produced by atropine & a
short time afterwards, in a lesser degree by
Physostigma is assisted in the character
of the movement & form of the process
When human or Rana's blood is examined in
a 1 or 2% solution of atropine the [illegible]
[illegible] added with [illegible]
blood. In examining the process most closely
it may be seen that they do not consist of an

5

covering membrane with perfectly clear content
such as would arise from a process of imbibition, & such as we may
but that the structure is uniform throughout
produce

4

The corpuscles are commonly spherical at first 4

facts may be observed, — (Sometimes ^when the specimen is under^ immedi-
ate in the ^care of the blood^ necks) but ~~usually~~ (?) after ^the lapse of^ a few min-
utes ~~in the human blood~~ movements of a peculiar
kind ~~commence~~ ^begin^ characterized by the protrusion
of clear hyaline or very dimly granular processes
varying in shape ^some^ ~~from~~ small & bud-like ~~projections~~
others large & tuberous others again ~~than~~ encir-
cling a portion of the circumference like a hernia
membrane; but ^however they may differ in^ whatever the form they all pre-
sent the common features of a rounded contour
& a ^more or less^ hyaline aspect; Their number ~~may vary~~ from
~~numerous small ones surrounding~~
~~or two~~ large ones ~~are different~~ ~~to a corpuscle~~ to one
or two large ~~ones~~ connected with a single corpuscle
is never constant however but as a general rule the smaller
they are, the more numerous do they become, & in
this form often surround the circumference, in
a circlet of small blebs, but the most typical form
presents one or two large sized processes.
The outline of the corpuscle may change two or
three times within the minute by ~~from~~ the pro-
trusion & withdrawal of these processes.
It is to be remarked that
The corpuscles are not flattened but ^& do not adhere to the covering^ ~~assume~~ the
spherical shape, as may be well seen when on
touching the covering glass with the needle you cause
them to roll over, the appearance then presented
is that of a sphere studded with irregular
knobs. In examining the processes more closely
it may be seen that they do not consist of an

investing membrane with perfectly clear contents
such as would arise from a process of [illegible], & such as we may
but that the structure is uniform throughout
produce on them with water &c
very clear when compared with the body of
the corpuscles, yet dimly granular in the
clear field of the microscope

As you watch a corpuscle & see these clear processes thrown out
you are inevitably reminded of similar appearances [illegible] seen
in most of the Rhizopods. They present the same clear protopla

large and usually very active. The solutions were of
Sulphate of Atropia in Saline (2) solution (1/2 (1) %)

The action is characterized by the protrusion of clear, hyaline or granular processes, which also are-

~~for motion~~ of such a nature apart ~~from vitality~~ is unknown

Now though these movements characterised by the protrusion of portions of the corpuscles, vary greatly under different circumstances, both when removed from the body and, as we may believe, by conditions existing arising in the animal itself; yet in all as far as they have been traced, the processes which result ~~from the movement~~ are of a certain character viz irregular, acuminate, and, in ~~appearance~~ structure like the corpuscle itself. In this point, the white corpuscle differs from protoplasmic masses forming some of the lower organisms such as Amoeba & in which two elements may be distinguished; one clear, transparent, motory — the ectosarc; the other, granular and passive(3) — the endosarc. In the course of some investigations, undertaken with a view of ascertaining whether an antagonistic effect could be produced on the white corpuscle between Atropine and Physostigma a very definite important and interesting ~~effect~~ action of the both former reagent upon them was discovered, which forms the subject of the present communication. When we examine ~~the blood of any animal~~ in a dilute saline solution or serum, the characteristic movements of the white corpuscles are readily seen, caused by the protrusion at different points, of processes. For the observation newts blood was taken as the white corpuscles in it are both large and usually very active. The solutions were of Sulphate of Atropia in Saline(2) solution (1/2(1) %)

Among the ~~various~~ numerous substances reagents which have a marked definite action on ~~the~~ blood corpuscles, few definitely affect the colourless, ~~i.e. principally the red~~

(~~again~~ the action (2 [illegible] of reagents (which have in themselves active properties) is usually such, that in producing their effect they destroy the vitality of the corpuscles and it is through physical changes alone that the effect is recognized)

It may be readily understood (1) that the vital properties of such delicate ~~organisms~~ elements as ~~white~~ blood corpuscles would speedily be destroyed if removed from those conditions with which they are usually surrounded, far more so when exposed to some reagent capable in itself either through its physical or chemical properties of altering ~~it~~ them or annihilating.

It is indeed surprising that such delicate organs should under some conditions retain their vitality so long

In determining the vitality of the red corpuscles we have no ~~definite~~ data to go upon, but with the white it is different; here there is a factor absent in the former, ~~universally~~ invariably present, viz the power of spontaneous movement and while this continues it ~~gives evidence~~ may be assumed that Life exists though its absence the converse is no proof of death in a [illegible] proof of death

The action is characterized by the protrusion of clear, hyaline, or granulous processes, which also present blunt extremities and a sharply defined contour. Sometimes a distinct boundary line may be traced between the corpuscles and the process, in others a gradual blending of the two is observed The rapidity with which, ~~they are protruded & retracted~~ the action is produced varies somewhat, though in no definite ratio, with the strength of the solution. If the blood be first mixed with saline and the atropine solution afterwards drawn through the cell ~~motion~~ is slower in commencing, as it has not only to replace the normal movements, but its strength is diminished by the saline On the other hand if the blood is put at once on the slide with the atropine solution without saline and looked at immediately, many of the corpuscles may even then be seen with hyaline processes, though by this method the majority of them assume at first rounded forms and it is not till some time has elapsed that the action becomes general

for a longer or shorter period, some circumstance or other very greatly, under different circumstances - a slight increase in the temperature for instance, delays their movement.

power of spontaneous movement and while
thus continues it may be assumed
~~from evidence~~ that Life exists
though its absence may be proof of death

The various reagents which produce a definite effect on the blood corpuscles do so in nearly all instances through physical changes; these being recognized by alterations in form, constitution &c and occur at the expense of vitality.

The precise time when life ceases in ~~them~~ the colorless element ~~the blood~~ corpuscles we have no means of determining cannot accurately say but ~~in the colorless~~ we may assume ~~though~~ ~~corpuscles~~ the ~~exist~~ occurr-ence of movements ~~may~~ to be ~~taken as~~ a sure evidence of its ~~presence~~ existence, though ~~the~~ converse absence by no means always indicates their death, ~~(Whether~~ ~~for we may suppose changes of blood~~ changes of form ~~movements may take place~~ we may examine some corpuscles retain the spherical form for a longer or shorter period, some circumstance or other Now, though these movements vary greatly under different circumstances - a slight increase in the temperature for instance, determining their movement.

Among the numerous reagents which have a
marked ~~effect~~ action on the blood-corpuscles, very
~~few~~ definitely effect the colourless

the sulphate of atropia & the ~~blood of~~ colourless elements ~~used~~ employed were principally ~~the newt was chosen~~, those of the newt. ~~The method of investigation was as follows;~~ By the [illegible]; blood was taken from the newts tail and added to the solution, placed in a glass slip; the ~~precise~~ exact proportions between the blood and solution ~~was not~~ being accurately noted, but a ratio of one of blood to three was aimed at. In strengths ranging from

the following facts ~~have been noticed~~ were ascertained about the white corpuscles. In a longer or shorter time, varying somewhat with ~~the~~ solution, but rarely ~~extending~~ prolonged beyond fifteen minutes many of the corpuscles are seen to protrude, ~~clear pellucid granulous processes processes~~ buds which in form ~~may be~~ are usually tuberous or may extend as an uneven rim round the circumference margin, but never ~~as far~~ as I have seen, present the or even feebly the little shape & tenuity of the normal process

presenting a dimly granulous aspect on the clear field of the microscope

The movements may be continued for

These protrusions are thrown out ~~put out~~ & retracted oftentimes with great rapidity and at different quarters of the corpuscle, so that six or seven changes in form ~~outline~~ may occur within five minutes. Many at first present a circlet of small bleb-like projections, which after a time, increase in size and become active. The corpuscles are not flattened but usually assume a more or less spherical outline as is well seen when on touching the coverglass you cause them to roll over, the appearance then presented is that of a sphere studded with irregular knobs

If ~~you~~ are (2) examined ~~the~~ processes (1) more closely it will be seen that they do not consist of an investing membrane and perfectly clear contents, but that the structure is uniform throughout, very clear & hyaline compared with the body of the corpuscle, yet presenting a dimly granulous aspect on the clear field of the microscope

The movements may be continued for two or even three hours, gradually diminishing in frequency and number, till at last the corpuscles assume a round or slightly irregular form. Sometimes at this stage occasionally earlier corpuscles may be observed with a sharply defined semicircular or oval projection ~~extend~~ing from them. This must be distinguished from the processes above described as they are perfectly hyaline and are never retracted; though I have noticed and ~~described~~ recorded below a curious rotation of this projection about the circumference of the corpuscle. It would seem as if these later projections resulted from or were the altered remains of former ones, but they are by no means so general, the majority of the corpuscle become round and often show a nucle~~ar~~ visible condensation in their interior of their contents

(Here ~~add~~ insert the action on Human oo & the strengths found most favourable for ~~these~~ occurrences)

I must call attention to the fact that the ~~results~~ statements here ~~given~~ recorded are the results of a large series of observations; nearly every strength having been tried three or four times & some especially the 1/2 1 & 2 per cent. very many times. Discrepancies of an unaccountable nature sometimes occur in the effects produced by a definite strength, the rapidity ~~as for instance~~ ~~for example with a 1/2 %~~ of the movements being more evident at one ~~time~~ observation than at another. ~~too~~ However the accurate effect of successively diminishing doses though interesting, is not essential in such an investigation as this, where no attempt has been made as has been done in the case of [illegible] to render it of any therapeutical value. The interest is solely histological and the action is quite general & definite enough in spite irrespective of occasional variation.

After ascertaining that the action of Phy. alba on the white corpuscles was the same individual poisons not be suspected than any antagonism could be brought out. demonstrated

Some observations were however made with the results combined in different strengths, but no results followed, other than a continuation of the same action produced by either substance when given below

being small and pointed. However as Bacteria had developed in the solution it had probably had undergone some determining change before were very apparent

14/11/72

15

Physostigma

14

"Action of Physostigma and Atropia on the White blood Corpuscles"

Obs. 1 grs 12 (gr Pl 4th) per 1000 of saline. Action of the corpuscles almost stopped, only slight changes observed in the form, no processes were protruded

Obs 2 In another specimen several corpuscles were observed with processes, but the movements were very tardy

An appearance is noted in the nuclei (5) with regarding viz. a remarkable distinctness with irregularity in outline and also an increase of their number, as many as five may sometimes be seen

Obs 3 With same solution. No movements in any corpuscle could be detected after 20' although up to that time were of a very sluggish kind. The multinucleus appearance was well seen in this specimen

Obs 4th Same solution. In this specimen movements were observed throughout an hour, the processes being small and pointed. However as Bacteria had developed in the solution it had probably had undergone some deteriorating change

Nuclei were very apparent

98
32
66
5
9/330
98.36
9
5/882
176

98
5.
9/490
5.4
32
22

14/11/71

Physostigma

Obs 5 (a) Et. Physostigma 1½ % solution in saline
With this most of the corpuscle assumed
a rounded form, a few had pointed processes
but no movements of any kind were seen.

(b) Et. Physo. 2 %. No change whatever in the
corpuscles: they remain quite rounded with
a sharp outline and numerous nuclei in each

Obs 6. Phy (Et) 1% Corpuscles at first nearly
all rounded, but gradually small amabid
processes were protruded which continued
in action for over one hour & a half

Obs 7 Phy (Et) 2 % No change could be detected
in the corpuscles with this strength, they remained
either uniformly rounded or else slightly irregular
in other cases with well marked nuclei

[illegible] then saline process was observed and after
remaining stationary for a longer or shorter time

large pseudopodia were protruded. In this specimen after the lapse of nearly four hours some of them

Atropine

Obs 1. Atrop. Sulph. 1½ gr to 1000 measures of saline
The only point observed was that the movement continued exceedingly active

Obs 2. Atrop Sulph 2 3/10 gr to 1000 measures of saline
Excessive activity, the only thing noticed in a corpuscle watched 40'. On the addition of Phy. (gtt 12. per 100) a diminution of activity was observed and hair like processes were observed. Slight movement continued for over an hour

Obs 3. 1/2 % solution in saline
A very lively corpuscle was chosen, & kept under observation for two hours. the following was noticed up to 55' the corpuscle diminished in size, did not throw out any processes and nuclei became apparent in it. From 55' to 120' numerous clear hyaline processes were thrown out and retracted at various parts of the margins. Some of these were very large and as many as six or even seven could be counted in connection with a single corpuscle
About 1 hour from the first an irregular circlet of these hyaline processes was observed and after remaining stationary for a longer or shorter time

large processes were protruded. In this specimen after the lapse of nearly four hours some of the processes were still visible, though the corpuscles had evidently been dead some time
The length of time which elapsed before the clear processes were thrown out may be accounted for by the fact that the blood was in the first place put into a drop of saline and the atropine added round the edges: in this way it would take some time for the, through action of the reagent to be set up

Obs 4 1/2 o/o Atropia

Drop of blood in saline, reagent added afterwards
First 15' movements very active & locomotory processes accumulate. Second 15', still very active and one or two blunt hyaline processes may be seen. Third 15'. Most have taken on this action, often first apparent as small bleb-like projections completely surrounding the corpuscle all the corpuscles have a rounder outline than at first. Of two under special observation at 60' one still kept out the hyaline processes, the other had retracted all became round
At 80' Every corpuscle in the field (there were 14) except two present these hyaline processes, some as the smaller blebs others as the large pinnae processes. At 105' one of the remaining two showed were particularly active up to the first quarter of the second hour, when they became less so. Many of the processes remained

protruded, not being retracted, but changing their position, with regard to the corpuscle

the action. Corpuscle mounted at the same time with saline are in very active motion, the processes all spicate & dark

at 120' some had become round, but the majority still retained the processes in active change

at 150' The two under special notice have become quiescent - others are still active. In another preparation put up at the same time many corpuscles with large active processes were observed

after this the movements gradually ceased, most of the corpuscles became round, the hyaline prolongations having been retracted, though in a few they were still apparent

Obs 5- 1% solution; applied directly with no saline Hyaline processes were observed on several of the corpuscles at once; many of them not of such a very transparent aspect as in former occasions. On another slide prepared at the same time & dried at the same intervals a remarkable difference was observed in the action; for in this, though at first large clear processes were protruded, yet soon, all movements ceased, the corpuscles being evidently quite dead; while in the first the movements were particularly active up to the fourth quarter of the second hour, when they became less so. Many of the processes remained

protruded, not being retracted, but changing their position, with regard to the corpuscle

Obs 6 1% solution in serum of Spina bifida

On first examining some corpuscles presented the blunt other the sharp processes, while some are rounded with no movements Within the first 20' the corpuscles became very active and all showed processes, either of a very hyaline description or else a thick greyish protrusion. Many of these protrusions within half an hour had hyaline processes given from them. 75' Movements very active, both in the corpuscles on a slide with simple serum & in the one with atropine, but the difference in the character of the movements and processes is very well marked. At the end of one hour and a half, the movements became slower and at about two hours, had almost entirely ceased On another slide prepared at the same time great activity was observed at the end of three hours. In fig 2. at 190' changes are represented taking place in the corpuscle, but of what nature it is difficult to say From 110' to 165' it remained with a long blunt-pointed process protruded. Then a very hyaline process was thrown out

as of [illegible] was not retracted but the granular matter gradually overlaid it. Fig 3 represents a curious bottle-like

process which was completely withdrawn
The [illegible] [illegible] [illegible]
from the opposite end, and this, as shown in
the "figs", had in 45' minutes completely attend
its position, having traversed the whole circumfe-
rence of the corpuscle. The was not retracted, but
the long blunt process was: the corpuscle assuming
a rounded form

Obs 7 atrop. Sulph 2 % solution
Immediately on application most of the corp-
uscles assumed a rounded form, at the
same time throwing out clear processes.
Out of 15 corpuscles in the field, within five
minutes only three remained quiescent
Nuclei were apparent in many
Within 5' the corpuscle represented in fig 2
threw out six different processes, large & hyaline
and withdrew them. There is a greyish pellucid
wall about some of these & actly like the Ectosarc
of the Amoeba. In fig 2 at 35' three separate el-
ements could be observed. 1st the nucleus in
very distinct and figured. 2nd a granular
mass surrounding it & 3rd a clear hyaline ex-
pansion from it. Sometimes it appeared
as if this latter was not retracted but the
the granular matter gradually overlaid
it. Fig 3 represents a corpuscle with [illegible]

process which was completely withdrawn
The changes figured in fig 1. are very interesting
Up to 77' it continued exceedingly active, pro-
cesses being protruded & retracted much oftener
than shown in the sketch From 77' to 140' hardly
any motion was perceptible, beyond a slight
change in the outline of the processes
Fig 5. represents two corpuscles, that had been
quiescent for nearly an hour and now at
125' hyaline processes appear in each. What is
this? Is it physical or vital?
At 160' minutes the corpuscles were evidently
quite dead, though in one or two the processes
had not been retracted

Obs 8 Atrop. Sulph 2 o/o in Aqua destillata
Corpuscles at first all exhibited this characteristic reaction, but they looked very pale
In 15' the action of water was very evident in both the white & red corpuscles, the
former having became very pale & rounded.
the latter were also altered in shape & had lost
their colouring matter

repeatedly
(2) Another slide was taken with the Phy. alone
alone. When first looked at many of the corpuscles

had very amabid movements, but within 10'
all processes had been withdrawn; in some

Obs 9 (a) atrop. sulph 2%. Characteristic action going on

(b) Phy. (4l) 2%. Within 15' most of the corpuscles had become quite round, some a little granular, but no distinct movements could be seen. Nuclei were visible in many 25' No further action was visible. Fig 3 shows the appearance presented by most of them in 30'

(c) Slide with equal portions of 2% solution of each in it. Corpuscles present clearly the atropine reaction, but not to the same extent as with the atropine alone. This was within 30'; after this the action was much more marked and continued to be so, till after 80' had elapsed in spite of repeated flushings with the Phy. solution alone

(d) At 85' added solution of Phy (2%) to an atropin slide in which the movements were very active. The movements went on unimpaired, though the Phy solution was drawn through the slide repeatedly

(e) Another slide was taken with the Phy. solution alone. When first looked at many of the corpuscles

had very amabid movements, but within 10' all processes had been withdrawn; in some however, slight granular projections or little hair like proceses might be seen but these soon disappeared and within 25' more were with

(From the above we may draw the following conclusions. 1st, that white corpuscles in a 2% solution of Phy. (4L) soon die. 2nd, that when a 2% solutions of at & Phy are mixed, the characteristic action of atropine on the corpuscles is almost quite as evident as when no Phy is present. 3rd, that in an atropized specimen, in which the movements have continued for over an hour; they will not be stopped by the repeated flushing of the slide with 2% solution of Phy)

Obs 10. In a 2% solution of common salt; the white corpuscles soon shrank and became round, exhibiting no movements whatever

Obs 11 (a) 1% solution of each. and mii of Phy to mi of alsp used. Most of the corpuscles at first appeared round with many blebb like

ments still continued, but nothing like to such an extend as in ordinary saline.

Obs 12. In a 4% solution of atrop. sulph. the

projections from their surface, others had none
of them, while a few had the large hyaline pro-
cesses very well marked. Figs 1. 2. 3 represent these
three of figs 2. predominated. For half an hour
the activity of the movements seemed impaired
but after this as shown in fig 4. they went on with
great rapidity

(b) Phy 1%. Most of the corpuscles assumed
were
a rounded form, some a little nodular, while
others showed the amaeboid movements, though
sluggishly. At the end of 45' minutes slight
amaeboid changes could be noticed in a very
few of the corpuscles, the majority of which had
been long dead

These observations show, that, 1st in 1% solution
of each mixed in the proportion of 2/3 Phy to 1/3 atrop
the movements though retarded at first, go on
with rapidity within half an hour, when the
atropine reaction is perfected. 2nd that in a
1% solution of Phy (4/4) natural amaeboid move-
ments still continue, but nothing like to such an
extent as in ordinary saline.

Obs 12. In a 4% solution of atrop. sulph. the characteristic action is quite as well marked as in a more dilute one, continuing for over an hour

Obs 13. 2% solutions of atropia & Phy

(a) 3/4 Phy. solution to 1/4 atropine. In a large number of the corpuscles, the movements in this mixture were very tardy, at first, but afterwards as in fig 1 they became more active and exhibited the atrop. reaction much better

(b) 4/5 Phy to 1/5 atrop. Small bud like processes observed at first, but no great activity is noticed within 15'. In other parts of the slide very characteristic atropine corpuscle might be seen

(Conclusions from these are, 1st that corpuscles in 2% solutions (each 3/4 Phy to 1/4 at will continue to show the atropine reaction, 2. that in Phy 4/5 at 1/5 same solutions. the atropine reaction may be observed after the lapse of an hour, though at this time most of the corpuscle have become round)

and one corpuscle, particularly active was chosen for observation. As shown in the "fig" it continued

very lively. thinning out clear non granular proces

Obs 14 At & Phy (4t) 2% solutions of each in proportion of 5/6 of the latter to 1/6 of atropine

With this in neither of the two slides under observation did any very pit movements take place. Most of the corpuscles were either quiescent or the presumed slight granular irregularities ~~were observed~~ Some had very delicate small hyaline proceses but with the exception of one corpuscle no very evident change in outline could be seen: however in this one hyaline proceses were visible, being withdrawn and projected, though very slowly

This seems to prove that even this pactional quantity of atropine is sufficient to neutralize in a slight degree the action of the Physostigmia

Obs 15 Slide with 5/6 Phy 1/6 at. 2% solution of each after 15' at which time no distinct movement were discernable, only a little irregularities here & there among the corpuscles, the preperation was repeatedly flushed with a 2% solution of salt with the following result. At 30' several of the corpuscles had protruded hyaline rotten proceses and one corpuscle, particularly active was chosen for observation. As shown in the "fig" it continued

very lively. throwing out clear non granular processes and the corpuscle itself altering very much in shape being at one time quite hour glass shape At about 80' the corpuscle itself became round & the processes which previously had been attached at different positions on it, now appeared merged in one, which exhibited the following behaviour At 90' it was at the upper pole of the corpuscle and from that point it gradually shifted round the circumference, from left to right. occupying about 1' in traversing the quarter segment or nearly 5' in completing the circle At 105' there was a slight pause, and, without any change in the corpuscle, the movement became reversed, the direction being now from right to left. This continued up to 137' when it finally ceased and no further change was observed at 150'. What is this? Physical or vital? The process was very clear, sharply defined & showing no diminution in size or change in shape. The granular contents of the corpuscle within exhibited no motion whatever

From this observation we may conclude that, atropine will stimulate corpuscles to motion which are dying under the influence of Physostigmia

one which exhibits the same curious phenomena induced yesterday by the solution of abut

the circumference of the corpuscle. This was observed in several besides the one sketched. In one the

Obs 16. 5% Phy 4t. 1% Atrop 2% solutions of each

On prst examining the corpuscles looked round ded and the nuclei very apparent: some were a little irregular & had a few tiny hyaline buds, but no distinct movements could be detected

. 15', hyaline processes somewhat more evident- at 20' they were very marked in nearly all the corpuscles. These continued in action for over one hour and a half

Obs 17 Preparation of corpuscles in 2% solution of Phy (4t). left for 15' at which time no evidence of vitality could be detected in them. It was then repeatedly flushed with 2% solution of Atrop and carefully watched. 25' from the first flushing well marked processes were observed beginning to draw out/retracted. 45' Many in active motion, processes very hyaline, borders sharply defined 65' Most of the corpuscles have become rounded, smaller, have lost the multiple processes. Many however retaining one single large one which exhibits the same curious phenomenon as noticed yesterday viz the rotation of filamt

the circumference of the corpuscle. This was observed in several besides the one sketched. In one the movement was in the ~~horizontal~~ vertical not the horizontal plane

18 atropia 2% corpuscles very lively. Apparently two varieties of processes must be distinguished 1st the granulous, clear & hyaline when compared with the granular contents of the corpuscle but not like the 2nd; the perfectly hyaline ones in which even a dimly granulous aspect cannot be discovered. Both varieties may be observed in the one corpuscle

Obs. 19 Atr. & Phy 2% each 7/8. Phy. 7/8 atropia at 10' corpuscles devoid of processes or slightly granular. Under observation for 90' & no change whatever observed

Obs 20 Atr. & Phy. 2% 1/12 Phy 1/12 atropia after watching for one & a half hours. not the slightest change could be detected in the corpuscles they were all either oval or quite round

accurately measured, but about one fourth

The action of certain reagents — Atropia Physostigmia & Curare — on the Colourless corpuscles

The preparations used were the Sulphate of Atropia, a somewhat impure Sulphate of Physostigmia, kindly furnished by Prof Fraser of Edinburgh, and ordinary Curare, as obtained from Messrs Hopkins & Williams

Fresh solutions of Atropine were always employed. of the Physostigmia 1. c.c. of a 1 per cent solution was made at a time, and a rather larger quantity of Curare, one half per cent saline solution being used to dissolve them. The solutions were neutral or slightly alkaline

The blood employed was that of Man, Newt & Frog

The method of conducting the experiments was as follows: for the Newt & Frog the proportion between the blood and solution was not accurately measured, but about one part

the quantity of blood was added to the reagent on a slide and both carefully mixed, the surplus, after applying the coverslip, was removed with filter paper. For the human blood the proportion of four fifths reagent to one fifth blood was kept; both being measured in capillary pipettes. After mixing the preparation was surrounded with oil and maintained during observation at a temperature between 37°–39°C on a Stricker's stage or Mr Shäffers modifications of it

The experiments with atropia and Physostigma were undertaken with a view of demonstrating if possible in the white corpuscles, the antagonism ~~which~~ between these substances, which has been so ably shown to exist by Dr Frazer. In this – as you will hear – I have failed and am concerned cui

alone with the effects they produce

Sulphate of atropea in strengths between
1:2000, 1:2000, 1:1000 permits the normal
movements of the corpuscles to go on unchecked, though the
duration is somewhat diminished; still
even with 1:1000 some may be noticed in
motion after two hours application of the re-
agent. Solutions ranging from 1:1000 to
1:500 & 1:400 lessen the activity and dur-
ation of the amœboid changes, sometimes
altering them. Lastly in strengths between
1:500 and 1:100, 1:50, the character
of the movements and structure of the processes
are definitely altered.

The forms assumed by the colourless elements
depend on the protrusion of thread-like pl-
asmatic masses of protoplasm which in
their general aspect
structure and appearance are identical with
the body of the corpuscle from which they spring.
The alteration produced by atropea - acid as

I shall observe afterwards in a later degree by Physostigma — is as I said, in the character of the movement and structure of the process

When human or Newts blood is examined in a one, two or half per cent solution of atropia the following facts may be observed; The corpuscles are generally spherical at first, or not, they soon become so. After the lapse of a few minutes — movements of a peculiar kind begin characterized by the protrusion of clear hyaline or dimly granular processes, varying in shape & size, some small and bud like, others large and tuberous, others again encircling a portion of the circumference like a thin membrane, but however they may differ in this respect, they all present the common features of a rounded contour and a more or less hyaline aspect. The length of time which may ellapse before they become

apparent as never constant, but rarely extends beyond five minutes. Sometimes happens that immediately on touching you may notice the alteration, thus irreparably the cure with Keats blood, but it is minimal in the first observation to see some minimal processes, which are retracted before any change takes place. The number connected with a single corpuscle, according to their size, the smaller they are, the more numerous do they become and on this principle surround the circumference like a circlet of small blebs, but the most typical kind presents one or two large sized processes. The structure of the corpuscle may change two or three times within a minute, by their protrusion and withdrawal

A process under the microscope

It is to be remarked that the corpuscles are not flattened and adherent to the coverslip, but assume the spherical form; this is well seen, when on touching

is not always necessarily retracted at once, but may remain protruded a longer or shorter period. One only may be seen connected with a corpuscle & it may be watched for some time without any alteration in its shape or appearance. Again a corpuscle may remain quiescent & round for a variable time even a [illegible] without ~~protruding any~~ showing any signs of motion, but afterward the movement begins. Some never present these processes but remain ~~dormant & quiescent~~ motionless while others in the same field are changing rapidly. This however is not so remarkable as in examining an ordinary preparation of blood, not every corpuscle ~~in the~~ under observation moves some generally remain ~~motionless~~

It is much more common however for the large majority of the corpuscles to take in this movement a small minority only ~~remain~~ motionless presenting the variations described

the coverslip with a needle you cause them to roll over, the appearance then presented is of a sphere studded with irregular knobs

On examining the processes more closely, it may be seen that they do not consist of an investing membrane with fluid contents such as would arise from a process of imbibition, nor would the rapidity of their change be consistent with this view: but that the structure is uniform throughout very clear when compared with the body of the corpuscle, yet distinctly granular or glutinous looking on the field of the microscope. At the bases of the knobs, the boundary between them and the body of the corpuscle is sharply marked, but not in every case, a form of process may sometimes be seen which though commencing as a hyaline one, is by the rapid streaming into it of the granular particles of the corpuscle converted

into a blunt non-hyaline knob.

These occur with greater frequency in the more dilute solutions as 1:400, 1:500, but they may also be met with in the stronger

As you watch the disappearance of a process it seems to take place by its gradual absorption into the body of the corpuscle another one commonly being protruded at a different quarter, but this is never is not the invariable mode the process may not be withdrawn but its hyaline character may be obliterated by a granular change taking place into it

The Nuclei very commonly develop in the corpuscles after exposure for a short time to the reagent. This effect is more marked with Phyesostigma

Sometimes (2) you may see (3) in those cases where the line between the clear process & the body of the corpuscle is not sharply defined there succeeds elements, the nucleus in the centre surrounded by the granular mass, continuous with which is a clear non-granular process

Following this comes the action of Ammonia upon blood

(Sulphate of Physostigma)

Physostigma in strengths more dilute than below about 1:800 allows the normal movements of the colourless elements to continue for a variable time, the weaker the solution the longer do they remain amoeboid; a proportion of 1:1000 stops the movements within two hours. In Stronger solutions, that is from 1:800 to 1:300 there is causes almost a complete absence ~~cessation~~ of the ordinary processes ~~movement~~, the ~~what~~ movements that take place being of heaving undulating nature with occasionally a clear processes.

In Strengths between 1:300 & 2% produce the same changes as a like solution of atropia viz the protrusion of hyaline knobs, the chief difference being that the process in the former is ~~does~~ not ~~seen~~ so general, a larger number of corpuscles remaining quiescent. Otherwise the action of the two substances is identical

(Nature of the Process)

What is the nature of this peculiar modification in the movements and processes?

At first, judging from the strength of the solutions used and the poisonous nature of the reagents I was led to look upon these changes as a physical one but a closer examination of the processes, the mode in which they are rapidly shot out from different quarters of the corpuscle, the streaming into them of granules, the fact that waving undulatory movements may independently take place - all quite inconsistent with any physical view - have forced upon me the conclusion that it partakes of a vital character, as much so in fact as any movement in a protoplasmic mass does.

Processes such as I have described, devoid of any granules, clear & transparent, are the normal ones in many of the leucocytes ~~such protoplasmic masses~~ and as you examine the movements produced by [illegible] in the blood corpuscles you are invariably reminded of the ~~[illegible]~~ transparent ~~hyaline~~ processes met with in the Amoeba

If we seek a counterpart to this hyaline protoplasm

in the blood itself we find it in the granular white corpuscles. I would here remark in passing that I find there a much more constant element in human blood — in my own especially — than [illegible] by writers of them would have led ~~me~~ one to expect. Since my attention has been drawn to this point, I have rarely examined a specimen of blood without finding one or two. They consist of a clear protoplasm in which coarse dark granules are imbedded. It sometimes happens that these granules do not entirely fill — as it were — the corpuscle, a clear space, which especially when the (2) corpuscle is at rest & it is (1) in the centre, looks like a nucleus or a vacuole. ~~And~~ In some it may represent such but in the ones I speak of now, the granules are very sparse; & if you watch such a one in active movement spread out in the cover-slip you will see — as I have sketched in fig — the hyaline protoplasm usually forming the processes or undulating [illegible] formation, & into it the dark granules streaming

I believe the orthodox view of the structure of white ~~c~~ cor. is that they
~~The ordinary white corpuscles are supposed also~~
~~&~~ consist of a perfectly clear protoplasm in which ~~containing~~

On trying to determine the minimum percentage of atropia which would produce this effect on the white corpuscles, I was surprised to find that even in solutions so dilute as 1: 10,000 & 1: 15,000, though the normal amœbid processes were usually to be seen, & their activity in no degree impaired, yet occasionally a distinct hyaline process was met with on carefully going over the field. The quantity of atropine in these solutions being so infinitesimal, doubts arose as to whether there were in reality the reagent at all produced by ~~a minute amount of the reagent~~ or whether they occurred naturally ~~in contact the addition of the reagent~~. To determine this, I undertook the examination of specimens of Rats, Frogs & Human blood. Eighteen specimens in each were taken and a field ~~in~~ which contained a good many white corpuscles

To determine this I examined thirty six specimens of each kind of blood human newts & frogs. Eighteen without any reagent, eighteen with ordinary saline. A field medium was chosen on which the colourless elements were pretty numerous this was kept under close observation for 15'

In the human blood it was sometimes difficult to obtain many white corpuscles in the field at once when this was the case I kept under observation by moving the [illegible] [illegible] ones that [illegible] beyond its limits

The results are as follows

Newts blood	no reagent	144 examined	3 hy.	271.	7 hyaline
" "	in saline	127 " "	4 hy		
Frogs blood	no reagent	182	2 hy	319	& 6 hyaline
" "	in saline	137	4 hy		
Human blood	no reagent	90		187.	No hyaline
" "	in saline	97			

41

In the natural movements no differentiation takes place between this substance & the particles are imbedded [illegible] in the [illegible] exceedingly fine granules, but it seems after [illegible] and it would appear as though under the influence of these reagents portions of this ~~mass~~ matter might be protruded devoid of any granules, to be retracted again into the body or to lose its clear appearance by the flow of particles into it

This may occur normally in some white corpuscles
(these come about in Stricker's article)

Clear processes are mentioned I think by Binz as occasionally occurring under the influence of Quinine. I failed to produce any similar to those I have described with either the Sulphate or Hydrochlorate of Quinine or the Sulphate of Cinchonine. Hyaline processes are to be seen in the yolk spheres of the Batrachia. Blunt rounded processes are according to Golubew produced by electric stimuli.

Human blood with saline (continued

4 corpuscles in the field 4. "

3 " " " 3. "

6 " " " 6 "

5 " " " 5 "

In the human blood it was sometimes difficult to obtain many white corpuscles in the field at once as when this was the case I extended the ~~margin~~ of the field by keeping under observation corpuscles that were in reality outside its limits, by moving the slide

From the above it will be seen that in the blood of both the Newt and Frog hyaline pigmentations are to be met with, while none such were observed in the white corpuscles of Human blood. The number of corpuscles observed in the preparation presenting clear pigmentations is as follows

Newts blood no reagent 144, 3 Hyaline } 271. 7 Hyaline
" " with saline 127, 7 Hyaline }

Frogs blood, no reagent 182, 2 Hyaline } 319. 6 Hyaline
" " with saline 137 4 Hyaline }

Human blood no reagent 97 } no hyaline pigmentation seen
" " with saline 90 }

was chosen & kept under close observation
for fifteen minutes
Eighteen specimens were examined without
the addition of any saline & the same num-
ber with it, so that in all thirty six fields
of each blood were observed
The results are given below

Results Blood No reagent

10 corpuscles in the field 10, N
7 " " " " 7, N.
8 " " " " 8, N.
6 " " " " 5, N. 1, H.
9 " " " " 8. N. 1, H.
7 " " " " 7, N.
7 " " " " 6, N. 1 H.
9 " " " " 9, N.
10 " " " " 9a N. 1, H.
8 " " " " 8 N.
8 " " " " 8 N

Newts blood No reagent (continued)

6 corpuscles in the field 6. N.

5 " " " " 4, N, 1, H.

4 " " " " 4, N.

8 " " " " 8, N,

8 " " " " 8, N.

10 " " " " 10, N

12 " " " " 12, N,

Newts blood in ½ % Solution of Common Salt

8 corpuscles in the field 7, N. 1. H.

9 " " " " 9, N,

6 " " " " 5, N. 1, H.

6 " " " " 5, N. 1 H

9 " " " " 9, N,

7 " " " " 7 N.

8 " " " " 8 N.

7 " " " " 6, N, 1. H

6 " " " " 6, N.

Newts blood in saline solution (cont)

5 corpuscles in the field 5, N.
6 " " " " 5, N. 1, H
8 " " " " 8, N.
10 " " " " 8, N, 2, H
5 " " " " 5, N.
6 " " " " 6, N.
8 " " " " 8, N,
6 " " " " 5, N. 1, H
7 " " " " 7, N

Frogs blood. No reagent

8 corpuscles in the field 8, N.
10 " " " 9, N, 1, H
14 " " " 14, N.
11 " " " 11, N.
13 " " " 13, N.
10 " " " 10, N,
10 " " " 10, N

Frogs blood, no reagent (continued)

16 corpuscles in the field 16, N,
13 " " " " 13. N.
7 " " " 7, N.
11 " " " 10, N. 1, H.
8 " " " 8, N.
9 " " " 9, N,
6 " " " 6, N.
7 " " " 7, N.
8 " " " 8, N
12 " " " 11, N & 1, H
9 " " " 9, N

Frogs blood, in saline

9 corpuscles in the field 8, N. 1, H
6 " " " 6, N.
7 " " " 7, N.
4 " " " 4, N.
6 " " " 6, N,
H " " " 10, N. 1, H
10 " " " 10, N.
8 " " " 8, N.
7 " " " 7, N. 2, H.

Frog's blood with saline (continued)

9	corpuscles in the field.	8, N. 1, H.
8	" " "	7, N. 1, H.
5	" " "	5, N.
7	" " "	7. N.
6	" " "	6. N.
9	" " "	9. N.
12	" " "	11. N. 1, H.
6	" " "	5, N, 1, H.
7	" " "	7, N

Human blood without any reagent

6	corpuscles in the field	6, N.
5	" " "	5, N.
4	" " "	4, N.
8	" " "	8, N,
3	" " "	3, N.
4	" " "	4, N.
3	" " "	3. N.
5	" " "	5, N
6	" " "	6, N.
7	" " "	7, N.

Human blood without reagents (continued)

7 corpuscles in the field 7. R,
4 " " " 4. R,
8 " " " 8, R,
5 " " " 5, R,
7 " " " 7, R,
4 " " " 4, R.
6 " " " 6, R,
5 " " " 5, R,

Human blood with saline

4 corpuscles in the field 4, R.
3 " " " 3, R.
5 " " " 5, R.
4 " " " 4, R.
5 " " " 5, R.
6 " " " 6, R.
8 " " " 8, R.
4 " " " 4, R.
5 " " " 5, R
6 " " " 6, R.
6 " " " 6, R.
7 " " " 7, R.
4 " " " 4, R,
5 " " " 5, R,

The preparations used were, the Sulphate of Atropia, somewhat impure Sulphate of Physostigma, kindly furnished by Prof. Fraser of Edinburgh, and ordinary Curare, as obtained from Messrs Hopkins and Williams. Fresh solutions of atropine were always employed. Of the Physostigma, 1. cc. of 1/50 strength was made at a time, and a rather larger quantity of Curare. One half per cent saline solution was used to dissolve them.

The solutions were neutral or slightly alkaline

The blood of Man, Rat & Frog was used

The method of conducting the experiments was as follows:- for the Newts and Frog the proportion between the blood and solution was not accurately measured, but about one fourth the quantity of blood was added to the reagent on a slide, and the two having been carefully mixed, the surplus, after applying the cover-slip, was removed with filter paper

For the human blood the proportion of four-fifths reagent to one-fifth blood was kept both being measured in capillary tubes. After mixing the preparation was covered, and the cover glass surrounded with oil (Vaseline evaporates), and maintained during observation at a temperature of about 37°C - 39°C, by means of a warm stage.

~~by means of a Strethers stage or Von Schäffer's modification of it~~

The experiments with Atropia and Physostigmia were undertaken with a view of testing, if possible, on the white corpuscles, the antagonism between these substances

substances, which has been ~~partly~~ known ~~to exist~~ by Dr Fraser's work with regard to their action upon the auditory body, in this — as you will hear I have failed and am concerned now alone with the effects they produce

Action of Atropia — Dr Fraser's

Sulphate of atropia in strengths between 1:3000, 1:2000 & 1:1000 permits the normal movements of the corpuscles to go on unchecked although the duration is somewhat diminished; still, even with 1:1000 some may be noticed in motion an hour and a half or even two hours after the application of the reagent.

Solutions ranging from 1:1000 to 1:500 or 1:400 lessen still more the activity and duration of the amœboid changes, sometimes attenuating the processes

Apathy, in strengths between 1:400 and 1% 2%. 3%, the character of the movements the form and structure of the processes are definitely altered

the forms assumed by the colourless elements

elements depend on the protrusion of thread-like, filamentous masses of protoplasm; which in their general aspect are identical with the body of the corpuscle from which they spring. The alterations produced by Atropia and I shall afterwards show by Physostigmine - as I said - in the character of the movement and structure of the processes When human or brute blood is examined in a half one, or two per cent. solution of atropia, the following facts may be observed

most often

The corpuscles are generally spherical at first; or if not, they soon become so. After the lapse of a few minutes, movements of a peculiar kind begin, characterized by the protrusion of clear hyaline or finely granular processes, varying in shape and size, some small + bud-like, others large and tuberous, others again, encircling a portion of the circumference as a thin rim; but, however they may differ in this respect,

repect they all present the common
features of a rounded contour and
a more or less hyaline aspect
The length of time which may elapse before
they become apparent is never constant,
but rarely exceeds five or ten minutes
It sometimes happens that immediately
on looking may notice the alteration.
This is especially the case with newts Hord
but it is more usual on the first observation
to see some normal processes which are
retracted before any change takes place
The number connected with a single
corpuscle bears some relation to their size
the smaller the processes are, the more
numerous do they become, and in this form
often surround the circumference like a
circlet of small buds; the more typical kind
however, presents me or two large sized knobs
The outline of a corpuscle may change two
or three times within a minute by their
protrusion and withdrawal
A process once thrown out is not always
retracted

retracted immediately / at once / but may remain protruded a longer or shorter period. One only may be seen in connection with a corpuscle, & it may be watched for some time without any alteration in its shape or appearance. Again some may remain quiescent and round for a variable time even with a 2% solution & afterwards begin the movements. Some never present these processes but remain motionless while others in the same field are changing rapidly. The usual [illegible] happens however that a large majority of the corpuscles take on these movements, a small minority only remaining motionless in presenting the above variations

It is to be remarked that the corpuscles are not flattened and adherent to the cover-slips, but assume the spherical form, this is well seen when in touching the cover-slips with a needle, you cause them to roll over, the appearance then presented is of a sphere studded with irregular knobs.

Or

On examining the processes more closely it may be seen that they do not consist of an investing membrane, with fluid contents, such as would arise from a process of imbibition, nor would the fact of their rapid change be consistent with such a view, but, that the structure is uniform throughout very clear when compared with the body of the corpuscle, yet dimly granular or glistening when in the field of the microscope

At the bases of the Knobs the boundary between them and the body of the corpuscle is sharply marked, but not in every case a form of processes may sometimes be seen, which, though beginning as a hyaline margin, by the rapid straining into it of granules converted into a blunt-run-hyaline thread

These occur with greater frequency in the more dilute solutions as 1:400, 1:800, but they may however also be met with in the stronger. These dark granular Knobs are sometimes protruded

Jun 6

independently of the hyaline processes
Again match the disappearance of a process
it seems to take place by its gradual ab-
sorption into the body of the corpuscle, an-
other one being commonly protruded at
a different quarter. This however is not
the invariable mode, the process may not
be withdrawn, but its hyaline character
may be obliterated by a fluxion of granules
taking place into it
Nuclei very commonly become apparent in the corpuscles
after exposure for a short time to the reagent:
this is still more marked with Phycoerythrin
In those cases where the line between the
clear process & the body of the corpuscle is
not sharply defined, you may sometimes
see three successive elements viz the nucleus
in the centre, surrounded by the
granular cell mass, continuous with which
is a clear hyaline process

The statements here recorded are the results of a large series of observations, nearly every strength having been tried three or four times, some especially the 1/2, 1 & 2 % very many times

Discrepancies of an inaccountable nature sometimes occur in the effects produced by a given strength, the variety of the movements &c. being more evident at one observation than at another

However the accurate effect of successively increasing doses, though interesting, is not so essential in such an investigation as this when no attempt has been made — as has been done in the case of Ammonium — to render it of Therapeutical value

The intent is solely Pathological and the action is quite general and definite enough in spite of occasional variations

Human blood. 1/5 blood 4/5 Sol–

	1:3000	1:2000	1:1500	1:1000	1:800	1:600	1:400	1:200	1:100
10'									
20'									
30'									
~~40~~ 60'									
90'									
120'									
150'									
180'									

Atropine

Human blood. Four parts solution one part Ths. blood

(1) 1. 2000

30' Normal movements
60' Continue very general
120' Still active
160' Many still in motion
180. Dead practically

(2) 1: 2000

30' Normal movements
60' " " " "
100' " " " "
150 Only a few still moving

(3) 1: 2000

15' Normal movements
40' " " " "
90' " " " "
120' Some have stopped but may of still in motion
170 None in motion

(4) 1:1500

30' Active amount of change.

60' " " " "

100' Not quite so active but still the majority still have processes.

130' Some in motion yet.

160' None with processes.

(5) 1:1000

10' Normal movements only

30' Still active

60' " " " "

100' Continue moderately active

130' Processes still to be seen but changing slowly

150' No movements

(6) 1:900

30' Normal movements only

50' Moderately active

80' Continue

120' An occasional process only can be seen.

140' No movements

(7) 1:800

15' Normal

40' " "

60 Still amatoid

90' Irregular projections to be observed in some, ~~then decidedly amatoid~~

100' " " "

120' Protuberances

(8) 1: 700

10' Many are protuberances then amatoid

30' Irregular protuberances as many, some normal

45' Sluggish changes in outline

80' There continue

100' Changes in outline, but no proper amoeboid movements

110' A few still more feebly

120' None to be seen in motion

(9) 1:600

15' A few only have distinct processes

30' Irregular changes in outline, not many distinct processes, Be in two hyaline processes seen.

75' Some still change, some not very clearly

100' All round.

(9) 1:200

(10) 1:500

10' almost all the corpuscles become round

20' a few irregular changes occur occasionally normal or hyaline process may be seen

60' these movements may still be seen

90' almost all are quiescent

100' no changes can be seen

(11) 1:400

20' the same irregular changes observed sometimes rapidly, but more commonly slowly accomplished.

40' an occasional amoeba or hyaline process may be seen

60' marked alterations in form still continue

80' none to

(12) 1:300

10' hyaline processes & irregular heaving movement to be seen on many; others quiet

30' " " " " "

60' a few only changing form

80' no movement to observed

(13) 1:200

Blunt nos - hyaline projection in many some hyaline others motionless

30' Hyaline processes more general

60' Slow alterations in form centime, with hyaline & granular knobs

75' No clear processes seen Some corpuscles still change a little

85' None seen in motion

(14) 1:100

10' Almost all the corpuscles present well developed hyaline processes

20' Centime

30' More active some that have not hyaline processes change their outline slowly

60' Majority motionless a few still in motion

90' No change to be seen

Atropine. Newts blood

(15) 1 : 50

10' The majority of the corpuscles have lost active processes

20' Continue moderately active

30' Some have become smooth others less activity

45' Very few to be seen in motion or with processes

(16) 4 0/0.

10' Well marked processes in many of the corpuscles

20' Continue, not very rapid in their changes

30' Hardly any to be seen

40' All motionless + round

(17) 6 0/0

10' No processes of any kind

20' " " " " " Corpuscle very granular.

Atropine. Newts blood

1 : 5000 Continue normally amaboid for several hours

1 : 3000 140' Have remained normal

1 : 2000 150' Some still actively amaboid

1 : 1000 30' Normal movements. An occasional hyaline process may be seen, but is rare

140' Still a few irregular alterations in some, the majority are however motionless

1:800

10' Corpuscles either normally amoeboid or rounded

25' An occasional hyaline knob has been seen, but normal processes or slow changes in outline predominate

60' }
80 } Continue. Some have become round. but
90 } majority still alter in outline

100 }
180 } Slow alterations only noticed.

1:500

20' A few hyaline knobs to be seen, but mostly the normal movements

60' Still a few of both kinds to be seen many however present undulatory movements having no distinct processes

90' Continue much the same

120' Still irregular changes

145' Very slight alterations in outline. Most of the corpuscles are rounded

1:400

20' Some amœboid, a few with hyaline processes, others with irregular changes

60' Hyaline & a few amœboid processes to be seen

100 Still in motion, processes of both kinds

1:400

1:400 (cont.)

120' A few may still be noticed in motion but sluggishly

140' No movements can be seen

1:200

15' Many mind, others still keep the slap nominal processes. A few blunt-clear knots

30' More of the clear processes to be seen

45' More general

80' Every corpuscle in the field — 14 = in minute present by slime knots, with large + small.

105' Still some clear projections to be seen

130' almost all quite motionless

1:100

10' Many clear processes seen at once
rest of the corpuscles unmade

25'
45'
60'
80' } Hyaline processes very general

90'
110' } Beginning less so, but still active movement

120'
130' } Only an occasional one seen, all unmade
+ motionless. Nuclei well developed

1:350

Some seen immediately on framing
10' 15' Corpuscles in the field, three to
seven: one in five minutes three
out six different processes
The movement continue much the same
at 20' 60' 70' 90', very perhaps a little
less active, the processes remaining out
45' None to be seen. all motionless

10%

10' Granules. Corpuscles irregular.

100'
120' } Movement very slowly accomplished
Sometimes at this period all movement has ceased, at another slight alterations can still be seen. As a rule, with this strength, the processes are most generally developed, & still marked, ceasing about the latter half of the second hour

4%

15': action well marked in many

30' Continues, they are less rapid in their alterations.

45': Only one or two with them. Most have become mud

60': Motionless

6%

10' Processes developed almost at once, change with some rapidity

20': Still some action, but many that had processes have become round

30': Only one or two with knobs. Not discernible

45': None to be seen. all motionless

1.0%

10' No change, corpuscles angular in form granular.

30' No movements

Frog poisoned with atropine & blood examined, while under its influence & after the death of the animal. No modification of the normal movements noticed.

Repeated with same result

Rent treated in same way. No change found in the blood corpuscles. Normal and abnormal changes in all

Repeated with same result

[illegible] is not so general, a larger number of corpuscles remaining

Physostigma

Sulphate of Physostigma in strengths more dilute than 1:800, allows the normal movements of the colourless corpuscles to continue for a variable time, the weaker the solution the longer do they remain Quiescent. A proportion of 1:1000 stops the movement in less than two hours. In stronger solutions i.e. 1:800 & 1:300 there is almost a complete absence of the ordinary processes, the movements that take place being of a heaving undulating nature with an occasional hyaline knob. Strengths between 1:300 and 1.2 & 3 percent produce the same changes as a like solution of atropia, viz the protrusion of hyaline processes, the only difference is that with the former - Physostigma - the action is not so general, a larger number of corpuscles remaining

quiescent; otherwise the action of the two substances is identical

The processes in Newts blood are much smaller as a rule, than the corresponding ones produced by atropin and summed the corpuscles

As to the effect of these reagents on the red corpuscles, nothing is perceptible till 2d when 1 & 2 % are employed. then curious markings due to exceedingly irregular inrolled tunes and cuppings of the surface of the corpuscle occur. In form these markings are triangular or as straight, or sinuously curved lines, sometimes the appearance is of little bright dots, but rarely two corpuscles are alike in both these respects

Physostigmine

Human blood. 1/500 4/5 Solut.

1: 3000: Normal movements continue almost unabated, for nearly ~~three~~ hours.

1: 2000. The same. Amœboid ~~processes~~ movements

1: 1000
15' Some round, the majority amœboid
30'
60' } Amœboid movements active & general
80'
100' appear somewhat less active
130' Almost all round & quiescent

1: 800
20' Processes not very distinct; irregular changes more prevalent. An occasional corpuscle seen ~~with~~ of an amœboid form.
25' Some are active, but changes in outline ~~are in~~ ~~two amœboi~~d more common than ordinary processes
50' Continue as above
70' Still alter but very slowly
100. No movements to be seen

1:600

15' Changes in nature slowly occurring
a few hyaline knobs. Many spots round

30' Corpuscles chiefly irregular in shape &
not very active. An occasional hyaline
process noticed

50' Slow alterations in nature still to be seen
in a few, the remainder motionless

65'. None seen in movement

1:500

20' Slow irregular changes have been going on
a few hyaline knobs, but all the corpuscles
very inactive

30' Continue the same

45'. Most of the corpuscles round & motionless
a few still present irregular processes
slowly changing

55'. No other movements to be seen

1:200

15' No very active movements, corpuscles
roiginla; with a few hyaline processes

30' Hyaline processes most common, in height
changes in pin predominate

50. Individual processes, same slow changes
take place, Many quite motionless

60' Nearly all have become quiescent

1:200

20' Hyaline knobs in many are formed

30' Still a number hyaline

40' A few irregular, majority round

55'. No other than changes

1:100

15' Hyaline knobs very general & moderately
active

26' Lessening in number & activity

35' Round corpuscles predominate

45' No movements can be seen

1:50

10' Process pretty well marked & changes with some rapidity

20' Continue but somewhat less active

35'. Hardly any to be seen, all the corpuscles stirred and motionless.

What is the nature of this peculiar modification in the movements and processes? At first, judging from the strength of the solutions used and the poisonous nature of the reagents employed it seemed most probable that the change was a physical one. Closer examination of the process, the mode in which they are rapidly shot out from different quarters of the corpuscle, the streaming into them of granules, the fact that undulating movements may coincidently take place - facts inconsistent with any physical view - have forced upon me the conclusion that it partakes of a vital character - as much so in fact as any movement in a protoplasmic mass does. Processes such as I have described, devoid of any granules, clear and transparent as the normal ones in many of the lower organisms, and as you examine the processes pro-

on the white corpuscles under the influence
of these reagents, you are inevitably reminded
of the clear protoplasmic masses forming
the pseudopods of some of the Rhizopods, as the
Arcellina Difflugia &c.

If we seek a counterpart to this hyaline
protoplasm in the blood itself, we find it
in the granular white corpuscles

I would here remark in passing that I find
there, a much more constant element in the
human blood — in my own especially — than the
scanty notice of them would have led one to
suspect. Since my attention has been drawn
to this point, I have rarely examined a specimen
of human blood without finding one or two
They consist of a clear protoplasm in which
coarse dark granules are imbedded
Sometimes it happens that these granules do
not entirely fill — as it were — the corpuscle, a
clear space is left, which, when it lies in the
centre, and the corpuscle at rest, looks like
a nucleus in a vacuole. In some it may
appear

pebrinent- such but in the ones I now refer to the granules are very sparse (at time there are rare compared with the ones which appear entirely filled with the granules) If you watch such a one in active movement, spread out in the cover-slip, you will see - as I have sketched in p 57 - the hyaline protoplasm forming the processes initiating the information & into it the dark granules streaming

All admit that the commun white corpuscle consists of a clear protoplasmic matrix densely crowded with small dark particles

In the normal movements or differentiation takes place between these two elements, both contribute alike in the formation of the processes

It would appear therefore that under the influence of atropia and Physostigma portions of this matrix might be protruded devoid of any granules to wether retracted again into the body of the corpuscle or to form its clear aspect in the flow of particles into it

I find
There clear processes may occur naturally
in some white corpuscles

In trying to determine the minimum per-
centage of atropia which would produce this
effect in human blood I was surprised to find that even
in solutions so dilute as 1:10,000, 1:15,000,
though the normal amoeboid processes
always to be seen and their activity in no de-
gree impaired, yet occasionally distinctly
alive processes were met with in carefully
going over the field. The quantity of atropine
in these solutions being so infinitesimal, doubt
at once arose, whether there were in reality
produced by the reagent at all or whether
they occurred naturally
To determine this I examined thirty six speci-
mens of each kind of blood - Human, Rat & Dog,
Eighteen without any reagent, eighteen in ordinary
saline. A field in each case was chosen in which
the

Colourless elements were pretty numerous and kept under close observation for fifteen minutes.

In the human blood it was often difficult to obtain many white corpuscles in the field at once when this was the case by moving the slide I noted, others invariably outside its limits.

The results are as follows

Newts blood - no reagent: No. examined 144; 5 hyaline
" " in saline " " 127; 4 " "
Frogs blood. no reagent " " 182 & 2 " "
" " in saline " " 137; 4 " "

That is

Newts blood. total number 271 with 9. hyaline
Frogs blood " " 319 " 6. "

Human blood no reagent 90 } 187 none hyaline
" " in saline 97 }

In these observations on the normal corpuscles all regular or irregular hyaline projections were noted whether small nipple-like, or broad & tuberous in fact, characterized by clearness in structure and

Intensity of nature, as distinguished from the common thread-like dark processes here which may be termed the natural hyaline processes of Newts & Frog's blood, generally seen either surrounding the corpuscle as a circlet in which case they are small, or as a single process of a larger size; but in whatever form they appear identical with the ones produced under the influence of the above reagents. The difference girls viz, that while the latter change form rapidly the former often remain stationary for a considerable length of time

These processes are I think referred to by Kuz as occasionally occurring in solutions of Ammonia. I failed to produce any similar to those I have described with either the Sulphate or Hydrochlorate of Quinina or the Sulphate of Cinchonia. Hyaline processes are to be seen in the yolk spheres of the Batrachia

Colubrine mentions blunt knobs produced by chemic stimuli in the white corpuscles, they are however

not hyaline

After ascertaining that the action of Physostigma and Atropia on the colourless corpuscles was the same, it was not to be expected that any antagonism could be demonstrated between them

Some observations were however made with the reagents in different strengths, but no results followed, other than a continuation of the same action produced by either substance They are given below

Atropia & Physostigma 1% solution of each equal parts (Human blood)

10' well developed hyaline processes seen on nearly all the corpuscles

20' Still active. Outline of many corpuscles irregular and wavy; clear projections (bringing from them

40' Movements less evident. Many are round & motionless

5-6' No change in them. Nuclei well marked

Physostigma and Atropia 1/2 % solution of each. Equal parts (Human blood)

15' Changes in outline & small hyaline knobs seen in many

30' Still in movement. Nuclei very apparent

45' Outline much less general only an occasional clean process to be seen

60' No movements can be seen

Physostigma and Atropia, the former 1% the latter 1/2%. Equal parts (Human blood)

15' Processes very evident

30' Still to be seen also irregular non-hyaline protuberans

45' Changes in outline with a few clean processes noticed

60' Some of the corpuscles still irregular but no movement to be seen in them

Atropia 2% Physostigma 1% equal parts
human blood

15' Changes very marked & rapid Process
large

20' Continue in same others have become put
rified

30' Very few to be seen with clear processes the
large majority are quite round & motionless

35' No processes to be seen

"Curare"

When trying the effect of different reagents on the blood with a view of ascertaining whether the reaction with atropia and Physostigma was limited to them or more extended, Curare was suggested and I have given below the effect of successive strengths on human blood so far as I know its action on the blood has not hitherto been recorded

Nothing very special pertains to its action Ameboid movements continue lessening gradually as the solution becomes stronger till about a 1/500 solution a few irregular changes occur and then the corpuscles die usually within fifteen minutes

Frog's blood were arranged & their blood examined No modification is demonstrable in the natural appearance of the corpuscles could be discovered

Curare is not perfectly soluble a large quantity of sediment is left the clear supernatant fluid was used in these experiments

1:5000

10' actively amœboid

30' } Cuticuæ moderately active
60' }

80' }
100' } " " "

120' Movements less general

130' Still some to be seen amœboid

150' Almost all are motionless

170' No processes to be seen in any

1:1000

15' Amœboid processes but not very active

30' }
40' } Movements have continued pretty general
60' }

70' }
80' } Some of the corpuscles - the minute - are motionless

90' }
110' } Amœboid changes continue still but slowly

120' }
130' } Only occasional changes in these but the
corpuscles are quite round

They appear to get very thin & flattened before the
movements finally cease

1:800

15' Anabroid

30' Still active, some irregularities in outline with no distinct processes

50' Corpuscles still changing, but hardly so actively

70' Have continued in movement, Become have become rounded.

80' Pseudopodial processes, but moving slowly, others anabroid

90
100 } Movements diminishing in vigor, many motionless

110' Hardly ought to be seen in motion

1:500

10' Processes seen on part of the corpuscles, others rounded

20' Pretty active, more so than at first

35' Continue

~~60~~ Moving more visibly

65' Still in motion, some have settled down the process

75' Continue not very anabroid

100' almost all motionless and rounded

1:400

15' Awakened

30' Curtume pretty active

40' Action less general

50' The majority are mvd. others in sluggish motion

65'. All mvd & molusles

1:200

15' Some have been in sluggish awakened motion

20' a few still were moving

30' An occasional change in attitude to be seen

35' No further alterations

1:200

10' Many - the majority - are quite mvd. a few are awakened

25' One or two still in motion

30' No movement to be seen. Corpuscles appear somewhat flattened some irregular but motionless

1:100

5' almost all round, a few only with normal processes

10' Still one or two with processes but hardly any movement in them

20'. None to be seen with any processes.

92 (white)